

METHODS OF FORMING PROTEIN-LINKED LIPIDIC MICROPARTICLES, AND COMPOSITIONS THEREOF

ABSTRACT OF THE DISCLOSURE

5 The present invention provides for lipid:nucleic acid complexes that have increased shelf life and high transfection activity *in vivo* following intravenous injection, and methods of preparing such complexes. The methods generally involve contacting a nucleic acid with an organic polycation to produce a condensed nucleic acid, and then combining the condensed nucleic acid with a lipid comprising an amphiphilic cationic
10 lipid to produce the lipid:nucleic acid complex. This complex can be further stabilized by the addition of a hydrophilic polymer attached to hydrophobic side chains. The complex can also be made specific for specific cells, by incorporating a targeting moiety such as an Fab' fragment attached to a hydrophilic polymer. The present invention further relates to lipidic microparticles with attached proteins which have been first
15 conjugated to linker molecules having a hydrophilic polymer domain and a hydrophobic domain capable of stable association with the microparticle, or proteins which have been engineered to contain a hydrophilic domain and a lipid moiety permitting stable association with the microparticle.